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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,597	10/28/2003	Frank Himmelsbach	01-1410	5362

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
05/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/695,597	HIMMELSBACH ET AL.	
	Examiner	Art Unit	
	/Mark L. Berch/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-8* is/are allowed.

6)☒ Claim(s) *9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/10/2008 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for obesity and Type II diabetes, does not reasonably provide enablement for type I diabetes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Pursuant to ***In re Wands***, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples;

and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see ***In re Vaeck***, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims. Because of the broad scope of the 4 primary variables, billions of compounds are covered.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See ***In re Fisher***, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The dosage range information on page 54 is a 400 fold range, and does not take into account the weight of subject (normally, dosages are given in mg/kg). Moreover, this is generic, the same for the many disorders covered by the specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for type I diabetes.

(4) State of the Prior Art: These compounds are xanthines with a particular substitution pattern at the 7- and 8-positions. So far as the examiner is aware, no xanthines of any kind have been used for the treatment of type I diabetes.

(5) Working Examples: There are none for the treatment of any disease. There is a test showing that these compounds are inhibitors of DPP-IV, but this is not a standard test for type I diabetes, or osteoarthritis.

(6) Skill of those in the art: The skill level for the treatment for Type I diabetes is exceptionally low. Type 1 diabetes is an autoimmune disease that results in the irreversible destruction of insulin producing beta cells of the Langerhans islets in the pancreas. Despite the urgent need --- Type I diabetes is lethal unless the insulin is somehow replaced --- no pharmaceutical has ever been found effective against this disorder. Diet and exercise cannot reverse or prevent type 1 diabetes, although these are important in regulating the insulin given to the patient. Patients are treated either with insulin replacement therapy, or with transplantation surgery, either islet cell transplantation or, less commonly, pancreas transplantation. These do not treat the disorder per se, but only shield the patient from the lethal consequences. Patients may be given drugs for e.g. nephropathy or poor blood circulation in the feet, but these do not treat the disease itself, only the consequences of the lack of insulin.

The compounds claimed here are DPP-IV inhibitors. There is a DPP-IV inhibitor on the market, called Januvia™ (sitaglipin). Specific product information on this drug states explicitly that it is not to be used with patients having Type 1 diabetes. The reference "Patient Information JANUVIA™ "
<http://www.merck.com/product/usa/pi_circulars/j/januvia/januvia_ppi.pdf> downloaded from the internet 4/30/08 is presented as an example. This is in fact explicit evidence that not only is treatment of type-1 diabetes with DPP-IV inhibitors not enabled, it is actually contraindicated.

(7) The quantity of experimentation needed: Owing especially to factors 1, 4, 5 and especially 6, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. ***In re Wright***, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

The traverse is unpersuasive. Applicants argue, "Given the test showing that the claimed compounds are inhibitors of DPP-IV, a working example of the claimed compounds treating type-1 diabetes is not necessary for one skilled in the art to make and use the claimed invention without undue experimentation." The examiner has not said that a working example is "necessary", but rather, the fact that there is no working example, either with this disease or with an animal disease model is a factor to be taken into account in determining whether enablement exists.

Applicants next argue, "Symptoms of type-1 diabetes will be manifest sometime before a patient's insulin-producing pancreatic islets are totally destroyed and the patient will continue to produce insulin until the disease destroys all the patient's pancreatic islets." This is, in a somewhat narrow sense, true. Once over 90% of the beta cells are destroyed, the body is no longer able to regulate blood sugar levels and the patient develops some or all of the diabetes symptoms. So there would be that interval between 90% and 100% destruction. Applicants continue: "At least in this transition period between diagnosis and absolute insulin deficiency, it would be apparent to a skilled artisan that a DPP-IV inhibitor can be used to treat type-1 diabetes by promoting an increased serum insulin level." On what basis is this statement made? Are applicants stating that the drug

can retard the destruction of the remaining beta cells during that interval? If so, on what basis is such a statement made? If not, then the drug isn't really treating the disease itself, which is characterized by the destruction of the beta cells, but is rather helping the body cope with the disease by raising production in the last remaining beta cells. Moreover, what is the basis for the assertion that the drug can do this? In this regard, and to specifically rebut that notion, the examiner points to the above mention of the DPP-IV inhibitor which is specifically contraindicated for Type 1 diabetes.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Mark L. Berch/ whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300 for regular communications and (571) 273-8300 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

/Mark L. Berch/
Primary Examiner
Art Unit 1624

5/2/2008